REMARKS

These remarks are in response to the Final Office Action mailed September 15, 2010. Upon allowance of claims 1, 2, 5, 7 and 8, the claims directed to non-elected subject matter may be cancelled unless the Examiner believes rejoinder is available. Claim 1 has been amended to correct a grammatical error. No new matter has been introduced.

The Advisory Action indicated that the prior response was not considered. Accordingly, the following Remarks and the accompanying Affidavit are newly submitted.

REJECTION UNDER 35 U.S.C. §103

Claims 1, 2, 5, 7 and 8 stand rejected under 35 U.S.C. §103 as allegedly unpatentable over Hybridon (WO 99/27087) alone or in further view of TheRyte Limited (WO 99/42821). Applicants respectfully traverse this rejection.

As indicated in the prior response there is no mention in Hybridon (the primary reference) regarding the level of CDK1 and therefore there could be no understanding or contemplation of the ratio of CDK1 and CDK4. Hybridon discloses method for inhibiting the growth of a cancer cell which involves binding antisense molecules to the CDK4 gene so as to inhibit expression of CDK4. There is no mention of CDK1. There is no hint of suggestion in Hybridon that a cancer cell sample to be screened must comprise one or more cancer cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in a ratio of 0.6 to 1.6. Furthermore, Hybridon provides no teaching or suggestion that an effective agent is identified as one which alters the ratio in the levels of the CDK1 and CDK4 gene products in a cancer cell sample. The Examiner appears to consider that the Hybridon reference teaches that the antisense molecules described therein would inhibit the expression of CDK4 and would therefore alter the ratio of CDK1 and CDK4 gene products. This appears to be an inherency position by the Examiner. The Examiner is respectfully reminded that inherency requires that the inherent teaching being relied upon "necessarily flow" from the reference. As demonstrated below, this is not the case.

Hybridon does not mention CDK1, and certainly provides no teachings in relation to what happens to the levels of CDK1 on administration of the antisense agent. It is submitted that the inherent teaching alleged by the Examiner does not necessarily flow from Hybridon. For example, it is submitted that the concentration of CDK1 may decrease by the same amount as the concentration of CDK4 on administration of the antisense agent, leading to no change in the ratio of the levels of these two gene products as set forth by Applicants' claims. In support of this position the Examiner is directed to Figure 1A of the accompanying Affidavit by Dr. Warenius, which shows the effect at 2, 24 and 48 hours on the CDK1/CDK4 ratio of the well known anticancer agent cis-diamminedichloroplatinum (CDDP) on 2780, HRT18, MGHU-1 and RT112 cancer cell lines, each treated at a CDPP dose which reduces cell survival to 10%. Furthermore, Figure 1B (see the accompanying Affidavit by Dr. Warenius) shows that CDDP is effective in killing the cancer cells. It can be seen that CDDP is an effective chemotherapeutic agent, but does not alter the ratio of CDK1 to CDK4 gene products significantly, and the ratio remains within the range of 0.6 to 1.6 throughout the course of the experiment. Thus it is clear that not all chemotherapeutic agents alter the ratio of CDK1 to CDK4 gene products and thus the alleged inherent teaching relied upon by the Examiner *does not necessarily flow* from the Hybridon reference (see also, the Affidavit accompanying the response). A person of ordinary skill in the art would have no reason to consider that the antisense agent disclosed in Hybridon would alter this ratio.

Accordingly, the claims are non-obvious in view of Hybridon alone.

The claims also stand allegedly unpatentably over Hybridon in view of TheRyte. Again, nowhere in TheRyte is the person of ordinary skill in the art taught that a cancer cell sample can be identified as one which consists of one or more cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6. The Examiner alleges that TheRyte discloses that for cancer cells with mutated p53 the CDK1/CDK4 ratio is approximately 1.2 and for cancer cells with wild type p53 the CDK1/CDK4 ratio is between 0.6 and 1.3. We believe that the Examiner arrives at these numbers from Figure 5 and 6 by taking on efforts to construed the figures based upon hindsight using the present application as a

template. In fact, this is supported by the fact that nowhere in TheRyte is there any mention of a ratio of CDK1 to CDK4. The only place where this ratio is shown to be important is in Applicants' disclosure. It is submitted that Figures 5 and 6, at most would have taught the skilled person that there is a correlation between CDK1 and CDK4 levels in p53 mutant and wild type human cancer cells, but would not have led the person to believe that the ratio of these two gene products is important.

As set forth in the prior response, the entire body of the text of TheRyte teaches that a cancerous state can be identified simply by testing a sample from the ***co***-elevation of CDK1 and CDK4 (see claim 1 of TheRyte). It is submitted that there is no mention anywhere in TheRyte of the importance of the ratio of CDK1 to CDK4. The TheRyte reference teaches that CDK1 and CDK4 are useful as joint targets for drug discovery but in no way teaches the skilled person that an effective agent can be identified simply by determining whether the ratio of these two proteins had been altered.

The Examiner alleges that nowhere in the specification is it demonstrated that agents that are effective in the treatment of cancer alter the ratio of CDK1 and CDK4 gene products. Figure 2 (see the accompanying Affidavit by Dr. Warenius) shows Western Blots from Cdk1 and Cdk4 in protein lysates of RT112 bladder cancer cells. Western blotting is carried out by the method described in PCT/GB99/00506. The top panel shows a progressive increase in Cdk1 protein with time in the presence of the peptide agent PRGPRP, while in the presence of the peptide PRRPGP the amount of Cdk1 protein remains relatively constant. The bottom panel shows that the quantity of Cdk4 does not change significantly over time in the presence of either peptide. Thus it can be seen that in the presence of PRGPRP the Cdk1/Cdk4 ratio increases while in the presence of PRRPGP there is no significant change in the ratio. Figure 3 (see the accompanying Affidavit by Dr. Warenius) demonstrates that RT112 bladder cancer cells are killed by PRGPRP but not by PRRPGP, evidencing that an effective agent can be identified simply by determining whether the ratio of Cdk1 to Cdk4 has been altered.

For, at least, the foregoing reasons the claims submitted herewith are non-obvious over the references either alone or in combination.

For at least the foregoing, the Applicant submits that the claimed invention is patentable and request reconsideration and notice of such allowable subject matter.

The Director is authorized to charge any required fee or credit any overpayment to Deposit Account Number 50-4586, please reference the attorney docket number above.

The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

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